

### REMARKS

Claims 1-3, 5, 6, 8-14, 16, 30-34, 37, and 39-41 are pending and stand rejected. Claims 2, 9, 11, and 38 have been cancelled. Claims 1, 3, 8, 10, 12, 30, 32, 37, 39, and 41 have been amended. No new matter has been added by way of these amendments, and as discussed below, support for each amendment can be found in the original claims as filed and throughout the specification. Accordingly, the amendments discussed below do not require the Examiner to perform any additional searching. Reconsideration of the pending claims is respectfully requested.

#### Objection to the Specification

The Examiner has maintained the objection to the specification for allegedly lacking complete continuity data in the first paragraph of the specification. Applicants acknowledge the objection raised by the Examiner and respectfully note that it is Applicants' right to claim priority to a previously filed application but not a duty. (See MPEP § 201.11, III. E.) The chain of priority presently recited in the first paragraph of the specification recites an unbroken chain of previously filed cases, which provide a basis for the presently claimed priority date of December 18, 1996. As such, Applicants need not recite a reference to international application PCT/US97/23014, filed December 12, 1997. Accordingly, Applicants respectfully request that the Examiner withdraw the present objection to the specification.

#### Claim 10 is definite

The Examiner has maintained the rejection of Claim 10 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for including the phrase "expression system for a cell-based detection system for a functional polyketide." Applicants have deleted the word "functional" Claim 10. Applicants submit that the subject matter of Claim 10 reciting an expression system for a cell-based detection system comprising at least one nucleotide sequence that encodes a polyketide responsive target for a polyketide clearly defines the metes and bounds of the claim. One of ordinary skill in the art would readily recognize that a polyketide capable of binding to a polyketide responsive target and eliciting a response from the target was "functional". Accordingly, deletion of

this term clarifies the subject matter of the claim. In view of this, Applicants respectfully request that the present rejection of Claim 10 be withdrawn.

Claims 30-34, 37, 39, and 40-41 are definite

The Examiner has maintained the rejection of Claim 30-34, 37, 39, and 40-41 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for reciting “a coding region of . . . a catalytic activity of a polyketide synthase”. Independent Claims 30 and 37 have been amended to clarify the subject matter considered by Applicants to represent the invention. Claims 30 and 37 have been amended to more clearly recite the components of expression vectors adapted for *E. coli* or yeast expression, wherein the vectors comprise a vector comprising a nucleotide sequence encoding a selectable marker operable in yeast or *E. coli*, and a polyketide synthase gene operably linked to a promoter operable in yeast or *E. coli*, wherein the product of the gene has at least one functional polyketide synthase catalytic activity and a recombinant expression system encoding a holo ACP synthase gene, the product of which is effective in the pantetheinylation of said PKS.

Claims 1, 3, 5, 6, 10, 12-14, and 40-41 are definite

Claims 1, 3, 5, 6, 10, 12-14, and 40-41 were newly rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for reciting the phrase “encodes for”, appearing in Claims 1, 10, and 12. These claims have been amended in accordance with the suggestion of the Examiner.

Claims 32, 34, 37, and 39-41 are definite

Claims 32, 34, 37, and 39-41 were newly rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for reciting a holo ACP synthase being effective in the pantetheinylation of the PKS because the limitations in Claim 30 allegedly did not require a PKS enzyme. In light of the amendments discussed above specifying a PKS gene, Applicants submit that this rejection is now moot.

Claim 41 is definite

Claim 41 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for reciting “ACPS”, which, as taught in Example 6, did not function. Claim 41 has been amended to remove the reference to ACPS.

Effective Holo ACP synthases were in possession of Applicants at the relevant time

The Examiner maintained the rejection of Claims 1, 3, 5, 6, 16, 32, 34, 37, 39, and 40 (newly rejected) under 35 U.S.C. § 112, first paragraph, for allegedly lacking an adequate written description. Specifically, the Examiner alleged in the final Office Action that one of ordinary skill in the art would not reasonably conclude that Applicants were in possession of the claimed invention at the time the application was filed. Applicants respectfully disagree.

The specification teaches what type of holo ACP synthases should be used with the claimed methods and teaches how to assay for ACP synthase activity. For example, the specification teaches that, “[i]n general, holo ACP synthases associated with fatty acid synthesis are not suitable; rather, synthases associated specifically with polyketide synthesis or with synthesis of nonribosomal proteins are useful in this regard.” (Specification, page 8, lines 3-5.) This statement indicates that effective holo ACP synthases typically are preferably those that are specifically associated with polyketide synthesis. The preference that an effective holo ACP synthase be one that is associated with polyketide synthesis indicates the subset of holo ACP synthases that are effective with the claimed invention.

Applicants submit that the state of the art at the relevant time period was replete with examples of effective ACP synthases as defined by the specification. For example, the International Union of Biochemistry and Molecular Biology (IUBMB) classifies enzymes into a variety of different categories. The IUBMB formed the category that comprises holo ACP synthases (EC 2.7.8.7) in 1972. This observation shows that the specification provides guidance to one of ordinary skill in the art to readily select from a number of ACP synthases to use in the claimed invention.

Applicants submit that the teachings in the specification that a preferred holo ACP synthase be specifically associated with polyketide synthesis coupled with the state of the art at the time the present invention was filed is a sufficient showing to allow one of ordinary skill in the art to reasonably conclude that applicants were in possession of the claimed invention at the time the application was filed. As such, Applicants request that the present rejection of the claims be withdrawn.

Claims 1, 5, 6, 16, 32, 34, 37, and 39-41 are fully enabled

Claims 1, 5, 6, 16, 32, 34, 37, and 39-41 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. Applicants respectfully disagree and submit that one of ordinary skill in the art would be able to practice the full scope of the claimed invention without undue experimentation. However, to advance prosecution of the present application, Applicants have limited the scope of independent claims 1, 8, 30, and 37 to modular (type I) and fungal PKS.

As discussed above, the specification of the present case teaches that it is preferable to use holo ACP synthases that are specifically associated with polyketide synthesis. (Specification, page 8, lines 3-5.) The specification also provides an assay by which a skilled artisan can determine whether a particular ACP synthase is effective in the pantetheinylation of a type I PKS. In particular, Example 6 provides detailed teachings to those of ordinary skill in the art regarding how to test holo ACP synthases for activity with a type I PKS.

Applicants submit that the significant amount of information available in the art regarding holo ACP synthases coupled with the teachings of the specification provide more than sufficient guidance to one of ordinary skill in the art to practice the claimed invention without undue experimentation. In view of these amendments and comments, Applicants respectfully request that the present rejection of the pending claims be withdrawn.

Claim 8, 9, 11, and 12 are novel

Claim 8, 9, 11, and 12 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Khosla *et al.* (U.S. Patent No. 5,712,146). To be anticipatory, a reference must disclose each and every limitation of the claimed invention. The rejected claims recite a modified recombinant yeast, *E. coli*, or plant host cell, which in unmodified form does not produce polyketides. Khosla *et al.* does not teach a yeast cell, *E. coli* cell, or plant host cell, which in unmodified form does not produce polyketides. At best, Khosla *et al.* teach a *S. coelicolor* strain (CH999), which in an unmodified form does not produce polyketides. However, this cell type is not a yeast, *E. coli*, or plant cell. Accordingly, Khosla *et al.* does not teach all the limitations of the claimed invention and therefore cannot be anticipatory. Therefore, Applicants request that the present rejection of Claims 8, 9, 11, and 12 be withdrawn.

The pending claims are not obvious in view of the cited art: Lambalot *et al.*, Shen *et al.* and Bierman *et al.*

Claims 1, 5, and 6 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lambalot *et al.*, in view of Shen *et al.* and/or in view of Bierman *et al.* To render a claim obvious, the one or more references cited against the claim must, *inter alia*, teach or suggest all the limitations of the claimed invention. Lambalot *et al.* is cited for teaching a host cell containing an ACPS gene with other genes for the production of a particular polyketide. The ACPS gene taught by Lambalot *et al.* is an ACPS gene that is associated and central with fatty acid synthesis. (See Flugel, *et al.*, JBC 275(2):959-68 (2000)).

As disclosed in the specification of the present case, the use of such fatty acid synthesis associated ACPS genes is specifically discouraged. This disclosure supports the amendment to Claim 1 that requires that the ACPS claimed not be associated with fatty acid synthesis (Specification, page 8, lines 3-4). By introducing this fully supported negative limitation into the claims, Applicants distinguish the claimed invention from the cited art. The teachings of Lambalot *et al.* are limited to ACPS associated with fatty acid synthesis and none of the other references cited

teach ACPS. As such, the proposed combinations of references does not support the obviousness rejections raised in the final Action. Accordingly, Applicants request that the obviousness rejections of Claims 1, 5, and 6 be withdrawn.

Claims 8 and 11-14 are not obvious in view of the cited art: Khosla *et al.*, Bierman *et al.*, and Oliynyk *et al.*

The rejection of Claims 8 and 11-14 as allegedly being obvious in view of Kholsa *et al.* in view of Bierman *et al.* or Oliynyk *et al.* was maintained because the Examiner correctly observed that *S. coelicolor* CH999 cells do not produce polyketides. Claim 8, from which Claims 11-14 directly or indirectly depend recites a modified recombinant a yeast, *E. coli*, or plant host cell, which in unmodified form does not produce polyketides. The claimed host cell differs from the host cells taught in the cited art. Specifically, Kholsa *et al.*, Bierman *et al.*, and Oliynyk *et al.* do not teach or suggest the claimed host cells. As such, neither combination of references teaches or suggests all the limitations of the claimed invention. As such, the proposed combinations cited against Claims 8 and 11-14 does not support an obviousness rejection. Accordingly, Applicants respectfully request withdrawal of these rejections.

#### Conclusion

Applicants have endeavored to address all of the pending issues raised in the final Office Action. In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 300622001610. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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